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CORRESPONDENCE
Coronary artery disease

'No research without perfect methods': a problematic approach in epidemiology

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Authors' response to the correspondence "The associations between dietary sodium and atherosclerosis. Are the methods used accurate and reproducible?" by Campbell NRC, published in European Heart Journal Open, oead110, https://doi.org/10.1093/ehjopen/oead110.

We have read the anticipated letter from Prof. Norman Campbell raising concerns about our use of the Kawasaki formula for estimating 24 h sodium excretion.

A major limitation to all research regarding salt intake is the lack of optimal method used to estimate the intake. To date, no perfect method exists to accurately capture the long-term salt intake, particularly given that an individual's salt intake substantially fluctuates during the life cycle, from day to day and from meal to meal. What generally is considered 'the golden standard', measurement of 24 h sodium excretion in up to seven non-consecutive 24 h urine collections, is not without major limitations. It is costly and highly inconvenient, making it unfeasible to use in large-scale epidemiological studies. The time-consuming burden for the participants yields a high drop-out frequency and non-complete collections, which will introduce a selection bias in the study material and relevant concerns regarding generalizability of results. In this regard, spot urine samples with estimations of the 24 h urine excretion have some obvious advantages. As pointed out by Prof. Campbell, food frequency questionnaires (FFQ) (and other recall registrations) are proven unreliable (and, as we believe Prof. Campbell is fully aware of), and the results from FFQs have not been used in the analyses investigating the association between estimated salt intake and atherosclerosis in our study.[1]

We also agree with Prof. Campbell and the referenced association's statements that the Kawasaki formula is not accurate enough to draw firm conclusions on the absolute level of salt intake of an individual or on a population level, and therefore, we have been careful not to do so. We cannot exclude that the Kawasaki formula can introduce a systematic over-estimation or under-estimation of the absolute level of salt intake of the population; however, any such under-estimation or over-estimation would not affect the conclusions drawn in our study. Prof. Campbell has a theory that the variables in the Kawasaki formula (except sodium) are main contributors to the associations of estimated salt intake and outcome. Since Prof. Campbell has suggested that a way of studying this matter is to put sodium to a constant value, we re-did the calculations with constant sodium value. This gave a non-significant result [for Coronary Artery Calcium Score: odds ratio (OR) 0.90 (0.67–1.2) $P = 0.479$; for carotid plaque: OR 1.06 (0.81–1.39), $P = 0.665$] indicating that it is the variability in sodium that is the major contributor to the associations found in our study. Any increased variability due to the limitations of estimating 24 h salt intake from a spot sample would bias our results towards the null, and consequently, it can be expected that the associations between salt intake and atherosclerosis would have been stronger with a more precise method to estimate salt intake.

The debate around spurious results from the Kawasaki formula is partly rooted in the possible J-formed shaped curve found in some previous studies.[2,3] A J-curved association suggests a possibility of a risk increase with a low intake of sodium, a hypothesis that has spurred a lot of previous controversy. In the present study, we found no indications of J-shaped association between salt intake and atherosclerosis.

We respectfully disagree with the opinions in the letter by Prof. Campbell, particularly for large population-based studies such as the SCAPIS study, where logistical constraints on participants, investigators, and funding may necessitate deviations from the gold standard approach. Applying the 'no research without perfect methods' approach supported by Prof. Campbell would have grave consequences not only for salt research but also for epidemiological research in general, and we firmly oppose it.

Data availability

The personal data in SCAPIS is of sensitive nature and therefore cannot be made freely available. However, by contacting the corresponding author or study organization (www.scapis.org) sharing of data can be arranged for reproducing study results and procedures.

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